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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/578,912	05/09/2006	Keiichirou Kai	1034232-000038	4449

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EXAMINER	
BLAND, LAYLA D	

ART UNIT	PAPER NUMBER
1623	

NOTIFICATION DATE	DELIVERY MODE
04/29/2009	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

ADIPFDD@bipc.com

Office Action Summary	Application No.	Applicant(s)	
	10/578,912	KAI ET AL.	
	Examiner	Art Unit	
	LAYLA BLAND	1623	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *16 January 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1 and 4-6* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1 and 4-6* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *12/8/2008*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on January 5, 2009 has been entered.

This Office Action is in response to Applicant's request for continued examination (RCE) filed January 5, 2009, and amendment and response to the Final Office Action (mailed January 8, 2008), filed January 5, 200 wherein claim 1 is amended, claims 2-3 and claims 7-8 are canceled. Applicant's declaration of Keiichirou Kai submitted December 8, 2008 under 37 CFR 1.132, is acknowledged and will be further discussed below.

Claims 1 and 4-6 are pending and are examined on the merits herein.

The following rejection of record in the previous Office Action is maintained.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1 and 4-6 are rejected under 35 U.S.C. 103(a) as being unpatentable over Tanaka et al. (Org. Biomol. Chem., 2003, 1, 2833-2839, July 9, 2003, of record) in view of Gross et al. (J. Am. Chem. Soc. 1983, 105, 7428-7435, of record).

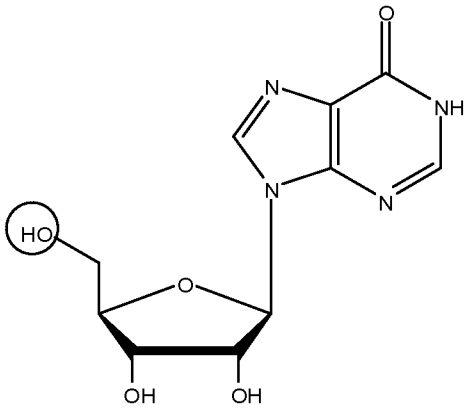
Tanaka et al. teach the phosphorylation of inosine to inosine-5'-monophosphate by nonspecific acid phosphatases from *Shigella flexneri* [page 2834, second paragraph]. The enzyme also mediates the phosphorylation of glucose to glucose-6-phosphate using pyrophosphate as the phosphate donor [page 2835, last paragraph]. The specific activity of acid phosphatase derived from *Sh. flexneri* was 40 U mg^{-1} [page 2834, first paragraph]. In the enzymatic phosphorylation of inosine, 40mM inosine, 100mM disodium pyrophosphate, and 0.1-1μM of enzyme solution in a total volume of 1 ml was used [page 2838, last paragraph]. For the glucose phosphorylation, the reaction mixture contained 1μM PhoN, 100mM glucose and 100mM disodium pyrophosphate in 100mM sodium acetate [page 2839, first paragraph]. The classical chemical introduction of a phosphate group into a polyhydroxy compound is tedious, and since such structurally different compounds as glucose and inosine are able to enter the active site of the enzyme and were successfully phosphporylated, this method has potential as an alternative to chemical methods [page 2837, paragraph bridging the first and second column].

Tanaka et al. do not teach the phosphorylation of a free pentose.

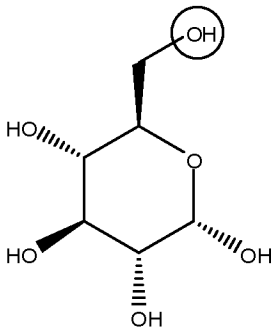
Gross et al. teach that ribose 5-phosphate is an intermediate in the synthesis of nucleotides, histadine and tryptophan [page 7428, first paragraph]. Methods for

preparing ribose 5-phosphate include obtaining the compound include chemical synthesis and enzyme-catalyzed synthesis using ribokinase [page 7429, Ribose 5-Phosphate].

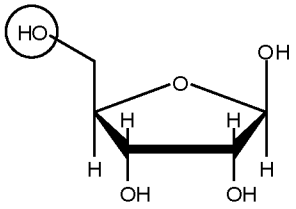
It would have been obvious to one of ordinary skill in the art at the time the invention was made to prepare a pentose-5-phosphate ester using acid phosphatase from *Shigella flexneri* in the presence of pyrophosphate. Tanaka et al. teach the selective phosphorylation of inosine (a nucleoside derived from a pentose) and glucose (a hexose). The skilled artisan would expect the corresponding reaction to proceed on a pentose in a substantially same or similar fashion because the structure of a pentose such as ribose is very similar to the structures of inosine and glucose with respect to the reaction sites, seen circled below. Further, Tanaka et al. teach that the enzyme is non-specific, and speculate that because it was effective for phosphorylation of inosine and glucose, that it might be widely applicable. The skilled artisan would have been motivated to prepare a pentose-5-phosphate ester because such compounds are useful intermediates in nucleotide synthesis, as taught by Gross et al., and are synthesized via chemical methods which Tanaka et al. teach can be replaced by methods utilizing acid phosphatase.



inosine



glucose



ribose

Response to Arguments

Applicant argues that substrate specificity of an enzyme is highly unpredictable. This argument is not persuasive because the enzyme used by Tanaka et al. is a nonspecific acid phosphatase, and Tanaka et al. suggest that, because the reaction was effective for substrates of very different structures, the reaction might have broader utility. Furthermore, as set forth above, the reactive sites of inosine, glucose, and ribose are all very similar.

Applicant argues that Ishikawa et al. teach that the presence of a hypoxanthine is important for recognition of inosine as a substrate for the reaction of an acid phosphatase. On the contrary, Ishikawa et al. (PTO-1449 submitted April 4, 2008) teach that "there is little interaction between the enzyme and the inosine base." (see page 542, first column) Further, it is known that the reaction proceeds on glucose, which lacks a hypoxanthine.

Applicant argues that, when the enzyme was modified by Ishikawa et al., to maximize the possibility of aromatic-aromatic interaction, the results were improved compared to the unmodified enzyme. This argument is not persuasive because the unmodified enzyme, wherein "there is little interaction between the enzyme and the inosine base," was also active. Thus, the inosine base is not required for activity.

Applicant's argument regarding the similarities between the enzymes from *Escherichia blattae* and *Shigella flexneri* are acknowledged. Thus, the skilled artisan would consider that if "there is little interaction between the enzyme and the inosine base" when the enzyme from *Escherichia blattae* is used, the same would be true when the enzyme from *Shigella flexneri* is used.

Applicant argues that pentoses consist of equilibrium mixtures of furanose and pyranose, and that the pyranose could not be phosphorylated because it lacks a primary alcohol. This argument is not persuasive because the furanose, also present, has a primary alcohol and does react, as illustrated by Tanaka et al.

Applicant argues that some pentoses and hexoses are phosphorylated using acid phosphatase, and some are not, and presents the declaration of Keiichirou Kai in support. The declaration provides evidence that, of 7 pentoses, 2 did not react; and of 8 hexoses, 3 did not react. This argument is not sufficient because a ribose derivative has already been shown to react, and the evidence in the prior art shows that the base is not required, as there is "little interaction" between it and the enzyme and a free hexose also reacts. Thus, the skilled artisan would have a reasonable expectation that

ribose would react. "Obviousness does not require absolute predictability of success." *Id*. at 903, 7"USPQ2d at 1681.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to LAYLA BLAND whose telephone number is (571)272-9572. The examiner can normally be reached on Monday - Friday, 7:00 - 3:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anna Jiang can be reached on (571) 272-0627. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Shaojia Anna Jiang/
Supervisory Patent Examiner, Art Unit 1623

/Layla Bland/
Examiner, Art Unit 1623